

The Discovery of the Molecular Structure of DNA - The Double Helix

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A Scientific Breakthrough



The sentence "This structure has novel features which are of considerable biological interest" may be one of science's most famous understatements. It appeared in April 1953 in the scientific paper where James Watson and Francis Crick presented the structure of the DNA-helix, the molecule that carries genetic information from one generation to the other. Nine years later, in 1962, they shared the Nobel Prize in Physiology or Medicine with Maurice Wilkins, for solving one of the most important of all biological riddles.

What is DNA?

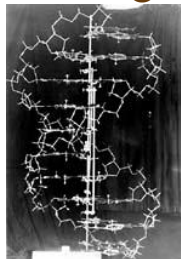


Francis Crick and James Watson

The work of many scientists paved the way for the exploration of DNA. Way back in 1868, almost a century before Watson, Crick and Wilkins, a young Swiss physician named Friedrich Miescher, isolated something no one had ever seen before from the nuclei of cells. He called the compound "nuclein." This is today called nucleic acid, the "NA" in DNA (deoxyribo-nucleic-acid) and RNA (ribo-nucleic-acid).

Two years earlier, the Czech monk Gregor Mendel, had finished a series of experiments with peas. Mendel was able to show that certain traits in the peas, such as their shape or color, were inherited in different packages. These packages are what we now call genes. For a long time the connection between nucleic acid and genes was not known. But in 1944 the American scientist Oswald Avery managed to transfer the ability to cause disease from one bacterium to another. What Avery had moved was nucleic acid. This proved that genes were made up of nucleic acid.

Solving the Puzzle

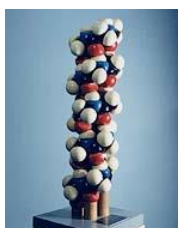


In the late 1940's, the members of the scientific community were aware that DNA was most likely the molecule of life, even though many were skeptical since it was so "simple." They also knew that DNA included different amounts of the four bases adenine (A), thymine (T), guanine (G) and cytosine (C), but nobody had the slightest idea of what the molecule might look like.

In order to solve the elusive structure of DNA, a couple of distinct pieces of information needed to be put together. One was that the phosphate backbone was on the outside with bases on the inside. Another was that the molecule was a double helix. It was also important to figure out that the two strands run in opposite directions and that the molecule had a specific base pairing.

Using X-rays to See Through DNA

Watson and Crick used stick-and-ball models to test their ideas on the possible structure of DNA. Other scientists used experimental methods instead. Among them were Rosalind Franklin and Maurice Wilkins, who were using X-ray diffraction to understand the physical structure of the DNA molecule.



A Three-Helical Structure?

The scientist Linus Pauling was eager to solve the mystery of the shape of DNA. In early 1953 he had published a paper where he proposed a triple-helical structure for DNA. Watson and Crick had also previously worked out a three-helical model, in 1951. But their theory was wrong.

Specific Base-Pairing

The base-pairing mystery had been partly solved by the biochemist Erwin Chargoff some years earlier. In 1949 he showed that even though different organisms have different amounts of DNA, the amount of adenine always equals the amount of thymine. The same goes for the pair guanine and cytosine. For example, human DNA contains about 30 percent each of adenine and thymine, and 20 percent each of guanine and cytosine. With this information at hand Watson was able to figure out the pairing rules. On the 21st of February 1953 he had the key insight, when he saw that the adenine-thymine bond was exactly as long as the cytosine-guanine bond. If the bases were paired in this way, the twisted ladder in the helix would be of equal length.

We All Share the Same Building Blocks

DNA is a winning formula for packaging genetic material. Therefore almost all organisms – bacteria, plants, yeast and animals – carry genetic information encapsulated as DNA. One exception is some viruses that use RNA instead. Different species need different amounts of DNA. For example, the DNA in *E. coli* bacteria is made up of 4 million base pairs and the whole genome is thus one millimeter long. The DNA of humans, on the other hand, is composed of approximately 3 billion base pairs, making up a total of almost a meter-long stretch of DNA in every cell in our bodies. In order to fit, the DNA must be packaged in a very compact form. In *E. coli* the single circular DNA molecule is curled up in a condensed fashion, whereas the human DNA is packaged in 23 distinct chromosome pairs.

Was Franklin Nominated

Many voices have argued that the Nobel Prize should also have been awarded to Rosalind Franklin, since her experimental data provided a very important piece of evidence leading to the solving of the DNA structure. In a recent interview in the magazine *Scientific American*, Watson himself suggested that it might have been a good idea to give Wilkins and Franklin the Nobel Prize in Chemistry, and him and Crick the Nobel Prize in Physiology or Medicine – in that way all four would have been honored. In 1958 however no one even nominated her - neither for the Nobel Prize in Physiology or Medicine nor in Chemistry.



The DNA-Helix

The two strands of the double helix are anti-parallel, which means that they run in opposite directions. The sugar-phosphate backbone is on the outside of the helix, and the bases are on the inside. The backbone can be thought of as the sides of a ladder, whereas the bases in the middle form the rungs of the ladder. Each rung is composed of two base pairs. Either an adenine-thymine pair that form a two-hydrogen bond together, or a cytosine-guanine pair that form a three-hydrogen bond. The base pairing is thus restricted. This restriction is essential when the DNA is being copied: the DNA-helix is first "unzipped" in two long stretches of sugar-phosphate backbone with a line of free bases sticking up from it, like the teeth of a comb. Each half will then be the template for a new, complementary strand. Biological machines inside the cell put the corresponding free bases onto the split molecule and also "proof-read" the result to find and correct any mistakes. After the doubling, this gives rise to two exact copies of the original DNA molecule.

The coding regions in the DNA strand, the genes, make up only a fraction of the total amount of DNA. The stretches that flank the coding regions are called introns, and consist of non-coding DNA. Introns were looked upon as junk in the early days. Today, biologists and geneticists believe that this non-coding DNA may be essential in order to expose the coding regions and to regulate how the genes are expressed.

Their mistake was partly based on Watson having misremembered a talk by Rosalind Franklin where she reported that she had established the water content of DNA by using X-ray methods. But Watson did not take notes, and remembered the numbers incorrectly.